

Histopathological Features of Mammary Gland Tumors in Native Domestic Female Cats from the State of Rio Grande do Norte, Brazil

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ABSTRACT

Background: There is in Brazil little information about histopathological features of feline mammary neoplasms. Especially in some Brazilian Northeastern locations such as Rio Grande do Norte (RN), there is complete absence of data regarding feline mammary neoplasm microscopy. Accordingly, this study aimed to describe the histopathology of mammary gland tumors in native domestic cats from the state of RN, Brazil.

Materials, Methods & Results: Records of 26 feline females, carriers of mammary neoplasms, were analyzed. Files from Veterinary Hospital of the Federal Rural University of Semi-Arid (located in the city of Mossoró, RN, Brazil) were used, comprehending the period from December 2004 to August 2009. The information collected was related to mammary tumor microscopic findings, obtained from classical histopathology reports. The lesions were distributed according to their biological behavior. Histological classification and morphological differentiation degree were also considered. Data related to neoplastic infiltration in adjacent tumoral regions were obtained as well. Descriptive statistic data were performed and submitted in percentage form. It was observed that most tumors (92%) exhibited malignant biological behavior. All of those were classified as carcinomas and, among the ones presenting benign behavior, intraductal papilloma was diagnosed. As referred to malignancies, the most common histological type corresponded to papillary carcinoma (42%). For morphological differentiation degree of mammary carcinomas, grade II presented the highest percentage (54%). Local tumor infiltration occurred mainly to the skin (75%).

Discussion: It has been reported that, among the palpable mammary masses in cats, 82% corresponded to malignancies and 10% were benign neoplasms. The data in discussion were not numerically equal to other researchers' results, although agreeing with them in the sense that most neoplastic proliferations of feline mammary gland exhibited malignant biological behavior. This knowledge becomes important when addressing a cat carrying mammary mass, although additional tests are needed to confirm malignancy diagnosis. The frequency for different histological forms found in the experiment under discussion showed divergence in comparison to values stated in the literature. However, there was consensus regarding results in relation to the greater amount of papillary patterns. Regarding morphological differentiation degree, there were similarities to other researchers' findings, which showed that the majority (57.8 to 60%) of feline mammary carcinomas belonged to grade II. Histological grading is a good parameter to stratify tumors according to their biological aggressiveness. Thus, this method is useful in the feline mammary neoplasia diagnosis, influencing the animals' prognosis and survival time. It was reported that 42% of cats presented located metastases related to mammary carcinomas, since the behavior of such neoplasms is characterized by invasion of adjacent tissues and metastases to distant sites. It has been mentioned that skin, soft tissue, blood and lymph vessel infiltrations corresponded to adequate prognostic factors for mammary tumors, on microscopic level. As for the data under discussion, tumor spread to the skin site was fairly frequent. This could be justified because of the intimate contact between tumor and adjacent skin. The results obtained in the study under discussion fill a gap in relation to mammary tumor histopathological findings in cats from the state of RN, Brazil, in addition to providing useful information for veterinary practitioners and veterinary pathologists which are active in the region.

Keywords: mammary neoplasms, histopathology, northeastern Brazil, *Felis Catus*.

INTRODUCTION

The number of domestic cats as pets in Brazil has been expanding over the years according to national population estimations [5]. In parallel, there has been an increase in cats' longevity. However, age expectancy increase is linked to onset of chronic diseases such as cancer [10]. Among tumors occurring in domestic cats, mammary neoplasms correspond to the most commonly diagnosed, reaching a value of 17% of all those animals' neoplasms [2,23].

International literature exhibits several works based on oncologic epidemiological studies on small animals, which provide important statistical data regarding histopathological aspects of the most prevalent mammary neoplasms. There is little information in Brazil about such data, especially with regard to the feline species, raising questions about whether the national sample is similar or not to the foreign one [26]. There are descriptions coming from certain federal units [1,6,22,25-27]. However, in other locations, mainly in the states belonging to the Northeast of Brazil such as Rio Grande do Norte (RN), there is complete information absence regarding feline mammary neoplasm microscopy.

Moreover, due to similarities between women mammary tissue proliferations and feline females, an investigation into pathological aspects of feline mammary gland injuries becomes important since the study of mammary neoforations in domestic cats can work as a model for comparative oncology [8,24,30]. In this sense, the present study describes the histopathological aspects (with emphasis on diagnosis and prognosis) of spontaneous mammary gland neoplasms of native domestic female cats from the state of RN, Brazil.

MATERIALS AND METHODS

Twenty six medical records of cats presenting mammary gland neoplasms were analyzed in retrospective way. The file used was from Veterinary Hospital of Federal Rural University of Semi-Arid (located in the city of Mossoró, RN, Brazil), comprehending the period from December 2004 to August 2009. The referred establishment offered medical-surgical care to animals from the municipality where it was located besides other regions of the state of RN. The information collected referred to microscopic findings in mammary tumors, obtained from classical histopathology reports, issued by an authorized laboratory. Lesions were distributed according to the tumors' biological behavior. Histological type and

morphological differentiation degree were also considered according to ratings already proposed by literature [9,18]. Data related to neoplastic infiltration in regions adjacent to the mammary tumor as lymph nodes, skin, and muscle tissue were obtained as well. Descriptive statistics for submitting data were performed in percentage form.

RESULTS

It was observed that most tumors (92%) exhibited malignant biological behavior, while the frequency of benign mammary tumors was only 8% (Figure 1). All malignancies were classified as carcinomas and those presenting benign behavior were diagnosed as intraductal papilloma (Figure 2). With regard to malignancies, the most common histological type corresponded to papillary carcinoma (42%), followed by tubular carcinoma (25%), solid carcinoma (21%), squamous cell carcinoma (8%) and solid tubular carcinoma at a percentage of 4% (Figure 3). Regarding morphological differentiation degree of mammary carcinomas, grade II possessed the highest percentage (54%), followed by grade I (25%) and grade III, at a frequency of 21% (Figure 4). Distribution of morphological differentiation degrees for histological types of the mammary carcinomas diagnosed was described in Table 1. Mammary carcinomas seemed to provide local neoplastic cell infiltration to certain areas, being skin the main affected region (75%), followed by regional lymph nodes (29%), and muscle tissue which showed an impairment frequency of 25% (Figure 5).

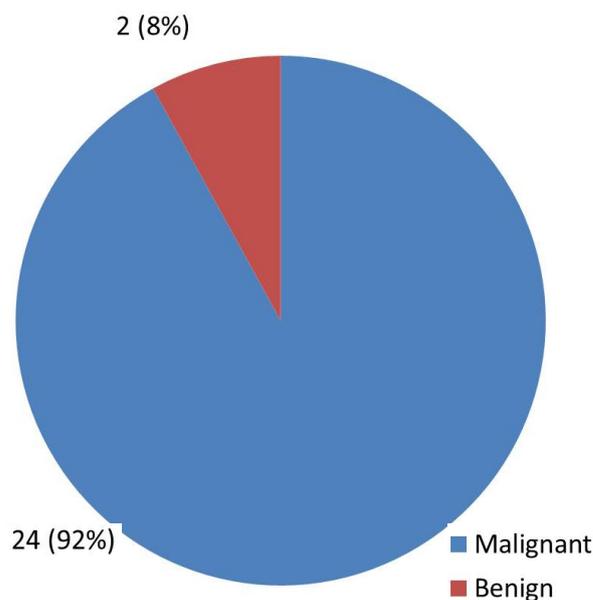


Figure 1. Neoplastic proliferation distribution of feline mammary gland according to biological behavior.

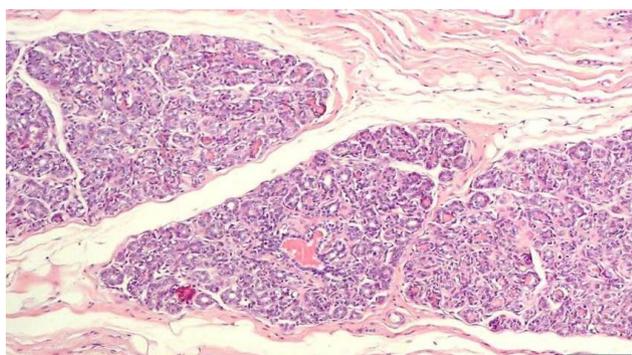


Figure 2. Histopathological photomicrograph of feline mammary intraductal papilloma. There was mammary duct proliferation forming nests, and scarce stroma tissue (HE stain, 10x). [Bar = 200 µm].

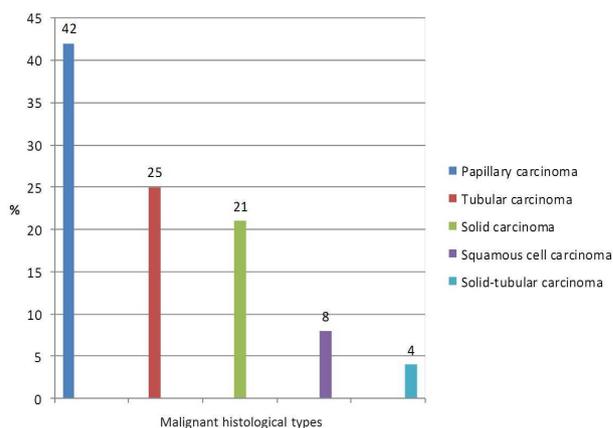


Figure 3. Percentage distribution of malignant neoplasm histological types of the feline mammary gland.

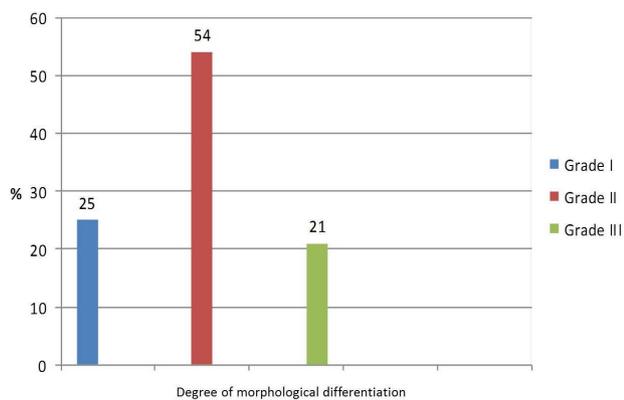


Figure 4. Percentage distribution of morphological differentiation degrees of malignant neoplasms of the feline mammary gland.

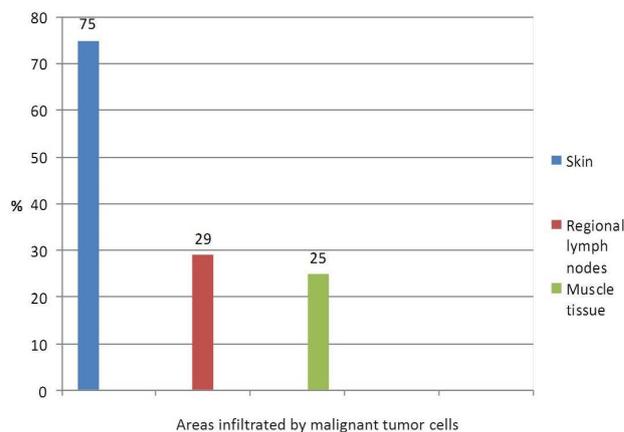


Figure 5. Percentage distribution of infiltrated regions by tumor cells adjacent to malignant neoplasms of feline mammary gland.

Table 1. Correlation between histological types of feline mammary gland malignant neoplasms and respective morphological differentiation degrees.

Histological type	Degree of differentiation (absolute and percentage frequency)		
	Grade I	Grade II	Grade III
Papillary carcinoma	01 (10%)	05 (50%)	04 (40%)
Tubular carcinoma	04 (67%)	02 (33%)	-
Solid carcinoma	-	04 (80%)	01 (20%)
Squamous cell carcinoma	-	02 (100%)	-
Solid-tubular carcinoma	01 (100%)	-	-

DISCUSSION

It has been reported that, among the palpable mammary masses in cats, 82% corresponded to malignancies and 10% were benign neoplasms [3]. It has already been found that most feline mammary lesions (72%) proved to be malignant, while benign tumors were related to only 10% of the total number [28]. Other authors found that 95% of domestic cat mammary masses accounted for neoplasms and all lesions showed malignancy [1]. It was also observed that the frequency of benign and malignant mammary tumors in cats amounted to 3.7% and 96.3%, respectively [7]. The data in discussion were not numerically equal to other researchers' results, although agreeing with them in the sense that most neoplastic proliferations of feline mammary gland exhibited malignant biological behavior. This knowledge becomes important when addressing a cat carrying mammary mass, although additional tests are needed to confirm malignancy diagnosis.

Ductal mammary papilloma is a rare injury in feline species [18]. In a study, only 7.7% of cases were verified, corresponding to the least frequent histological type among benign mammary tumors in domestic cats [28]. In another research, only 4% of the mammary tumors in cats showed benign biological behavior, while no case of papilloma was diagnosed, once the adenoma was the only benign tumor found [25]. In a retrospective data analysis, it was found that, among benign mammary neoplasms in cats, simple adenoma was the most prevalent (63.64%), followed by fibroadenoma (18.18%), complex adenoma (9.09%) and benign mixed tumor (9.09%), while, again, no cases of ductal papilloma was diagnosed [27]. Clinical presentation of the latter usually relates to presence of a small lesion, without adhering to deep layers and intact outer surface [10]. The only two cases of mammary papilloma observed in this study reinforced the unusual nature of this benign neoplasm in cats, being therefore in line with literature data. In women, mammary papillary proliferations are also uncommon, representing less than 10% of benign tumors and about 1% to 3% of all mammary biopsies [4]. Feline mammary papilloma has already occurred as an intraductal proliferation at the carcinoma periphery [28]. In humans, mammary papilloma significance cannot be underestimated due to the risk, not determined yet, of its malignant evolving; being likely the papilloma progression in invasive mammary carcinoma [4]. Although the present work

did not observe the association between papilloma and carcinoma, the papilloma initial diagnosis did not exclude the arising possibility of a later mammary gland carcinoma. Thus, for animals having already presented benign mammary neoplasms, the owners are recommended to perform mammary gland palpation every two or four weeks, besides semiannual medical evaluation [10].

A certain retrospective study of mammary tumors in cats found that carcinomas amounted to 92.3% of the cases, being tubular carcinoma the most common histological form, displaying a frequency of 36.1%, followed by papillary types (13.8%), papillary-tubular (11.1%), solid (11.1%) and cribriform (11.1%), still citing simple non-graded carcinomas (13.8%) and squamous cell carcinomas (2.7%) [6]. In other studies, the most frequently histological pattern observed in malignant mammary tumors was revealed as papillary-tubular carcinoma [3,26,27], while the least frequent was squamous cell carcinoma with a value of only 2% [3]. It was also reported that 32% of mammary carcinomas in cats were associated with two or more histological types [19]. The frequency for different forms found in the experiment under discussion showed divergence in comparison to values stated in the literature. However, there was consensus regarding results in relation to the greater amount of tubular and papillary patterns.

Squamous cell carcinoma represents the most common skin tumor in feline species [19], unlike the primary site in the mammary gland. Therefore, it is important to distinguish squamous cell carcinoma originating in the from histological types deriving from skin and its annexes, as well as squamous metaplasia associated with inflammation or metastasis from other sites [11,18]. Cases of squamous cell carcinoma of mammary tissue among the animals analyzed were few, in accordance with literature reports [3,6], although there being differences in percentage values. Thus, it was considered that this histological form possessed unusual or rare presentation in the feline mammary gland.

Although occurring in cats, World Health Organization classification does not recognize micro-papillary mammary carcinoma pattern either for felines or for canines. So, the same ends up being named as papillary or papillary-tubular. For this reason, and because there are no criteria for different architectural

pattern evaluation, several studies have reported papillary or papillary-tubular as the most frequent types of carcinomas [28]. This information is troubling, since it has been found that all cases of micropapillary carcinoma in the feline mammary gland were associated with clinicopathological characteristics of high biological aggressiveness and poor survival rate [24]. Thus, this neoplasm framework under the name of another histological form may underestimate the true severity of such a condition.

Regarding morphological differentiation degree, there were similarities to other researchers' findings, which showed that the majority (57.8 to 60%) of feline mammary carcinomas belonged to grade II, and grade I and III percentages ranged respectively from 12.7 to 28.9 and 13.3% of 27.3% [26,29]. However, in the present work, the value found for grade III was higher when compared to the research mentioned above. Three quarters of the mammary carcinomas in the study under discussion were classified between grades II and III. Thus, it was considered that the tumors analyzed had a higher potential for malignancy. Other authors also mentioned that moderately differentiated feline mammary tumors were the most frequent (60%), though the number of poorly differentiated tumors was high (27.3%) when confronted to the value (12.7%) of well-differentiated malignant proliferations [19]. According to certain studies, cats presenting grade III mammary carcinomas exhibited an average survival of only six months [28]. In cats, mammary tumor differentiation degree influenced postoperative outcomes in terms of prognosis [29]. The death rate one year after the mastectomy was 0% in cats with well-differentiated carcinomas (36 months average survival), followed by 42.4% for moderately differentiated carcinomas, and 100% for undifferentiated carcinomas [12,28,29]. For the cats in this experiment, which had poorly differentiated mammary carcinomas, their respective owners were guided on the severity of the condition and prognosis of each patient. Histological grading is a good parameter to stratify tumors according to their biological aggressiveness. Thus, this method is useful in the feline mammary neoplasia diagnosis, influencing the animals' prognosis and survival time [22]. Furthermore, it also suggests therapeutic modality choices as well as their respective intensities [26]. However, for the complete determination of the disease's progression prediction and its likely consequences, other factors were also considered [26].

When associating the descriptive classification and histological grading of feline mammary carcinomas, it was observed that papillary-tubular forms were distributed in 35.3% for grade I and 64.7% for grade II [26]. According to the same author, no papillary-tubular was framed carcinoma grade III (thus suggesting that this type possessed low malignancy), while solid carcinomas correlated with grade I (9.1%), II (63.6%) and III (27.3%), thus indicating a more unfavorable prognosis. The above quote was corroborated by other researchers in whose studies the cats with papillary-tubular mammary carcinomas revealed significantly higher overall survival when compared to those with solid carcinomas [29]. Mammary carcinomas with squamous differentiation comprised grades II and III, being regarded highly malignant, since there was no classification for grade I [26]. In the present study, the papillary-tubular form was not present, but, according to the above quote, the tubular and solid tubular carcinomas diagnosed were the least aggressive types, as most of them presented degree I and no samples exhibited grade III. Thus, these microscopic patterns can provide, in surgical and clinical routines, good prognosis, but correct treatment and proper monitoring of each patient are necessary due to risk of relapse, since it is a malignant neoplasm. The solid carcinoma was only distributed in grades II and III, being therefore targeted as a higher malignant behavior tumor. However, according to the histological grade, highlighting for marked tendency to malignancy was assigned to the papillary form, since it showed the highest percentage level among carcinomas classified as grade III. Therefore, one should pay special attention when faced with a histopathological report presenting such a mammary neoplasia morphological type. All unusual specimens of squamous cell carcinoma detected in the work under discussion possessed intermediate level of malignancy. Histological type and grade combination provides more accurate assessment to prognosis in feline mammary cancer [22].

It was reported that 42% of cats presented located metastases related to mammary carcinomas [15], since the behavior of such neoplasms is characterized by invasion of adjacent tissues, and metastases to distant sites [17]. It has been mentioned that skin, soft tissue, blood and lymph vessel infiltrations corresponded to adequate prognostic factors for mammary tumors, on microscopic level [20]. As for the data under discussion, tumor spread to the skin site was fairly frequent.

This could be justified because of the intimate contact between tumor and adjacent skin. It was also found that cell spreading ranged from skin epidermis into deep dermis. Constant observation of mammary tumor cells in the integument emphasized the importance of using proper surgical technique, in order to get the maximum margins of skin involved with the mammary tumor.

In metastasis developing, invasiveness amounts to the most reliable malignancy characteristic [14]. In literature, it was found that regional lymph nodes invasion, secondary to the feline mammary gland malignant neoplasms, was observed in a percentage from 21.5 to 42% [1,28]. Accordingly, in this study, the frequency of regional lymph nodes involvement was within the variation range demonstrated by other authors. The value obtained for neoplastic cell infiltration in regional lymph tissue was lower when compared to the percentage of tumor vascular invasion. This divergence could be explained by the fact that some cells that initially spread into the tumor stroma lymphatic vessels were destroyed by the host's defense mechanisms, having a small proportion reached the local lymph nodes. In bitches, it was observed that 10.5% of the lymph nodes examined presented metastases from the mammary carcinoma, contrary to what happened to cats which showed 60.2% of lymph node infiltration by neoplastic mammary cells [7]. These findings emphasized the idea of greater malignancy of malignant mammary tumors in the feline species [7]. The lymph node involvement pattern is usually dictated by pre-existing lymphatic drainage regional routes. The nearest nodes are often colonized earlier by tumor neoplastic cells [16]. For feline mammary carcinoma, axillary and inguinal lymph nodes are the most affected, although in some cases the sternal is also compromised [19]. It was described that cats with invasion into lymphatic vessels, resulting from mammary tumors were likely to metastases in regional lymph nodes. This finding was correlated with post-surgical survival reduction [19]. It was reported that all female feline with nodal metastases (secondary to mammary carcinomas) died in a period ranging from five to nine months [28,29]. Many authors have described lymph node involvement as an important prognostic factor for cats suffering from malignant mammary tumors [27]. However, obtaining of significant results may not occur by virtue of the fact that lymph node excision is usually performed only when their clinic involvement is evident [27].

It has already been verified that malignant mammary neoplasms in cats showed invasion to adjacent skeletal muscles in a frequency from 25% to 35.4%, varying according to histological pattern [28]. For this study results, neoplastic infiltration in skeletal striated muscle exhibited the minimum percentage value described in literature. Tumor extension into the abdominal muscles can be manifested simultaneously with regional lymph node involvement [1]. Due to this relationship, it is suggested that, during surgical procedure, being the mammary cancer adherence to the muscle observed, one must consider local lymph node removal. Extirpation must be performed even without any injuries, once there is the possibility of lymph nodes with neoplastic infiltration not revealing changes at gross exam [13]. It was cited that cats with large multiple mammary carcinomas presented higher rate of local metastasis. Thus, for these patients, one recommended maximum surgical margin obtainment, with the greatest possible excision amount of peritumoral tissue infiltrated by neoplastic cells such as skin, muscle, and lymph nodes [1].

Recently, Mammary Pathology II Meeting was held in Belo Horizonte, state of Minas Gerais, Brazil, where several abstracts related to canine mammary neoplasia were published. Those works reflected the efforts of several professionals from various public and private Brazilian institutions aiming to develop better protocols for the diagnosis, classification and prognosis, as well as treatments of canine mammary tumors [21]. This quote states greater attention given to the study of mammary cancer in bitches, in contradiction with domestic cats. Thus, scientific events of this nature, especially regarding felines, should be organized in order to contribute a greater amount of data to literature related to feline mammary gland cancer cases in several Brazilian states.

CONCLUSION

The results obtained in the study under discussion fill a gap in relation to mammary tumor histopathological findings in cats from the state of RN, Brazil, in addition to providing useful information (especially within the diagnosis and prognosis) for veterinary practitioners and veterinary pathologists, and even professionals involved with human oncology, which are active in the region.

Declaration of interest. The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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